AMENDMENTS TO THE CLAIMS

1. (Original) A pharmaceutical composition comprising a beta-blocker and an adenosine A_1 receptor antagonist (AA_1RA).

2. (Previously presented)The composition of Claim 1, wherein said beta-blocker is selected from the group consisting of acebutolol hydrochloride, atenolol, betaxolol hydrochloride, bisoprolol fumarate, carteolol hydrochloride, esmolol hydrochloride, metoprolol, metoprolol tartrate, nadolol, penbutolol sulfate, pindolol, propranolol hydrochloride, succinate, and timolol maleate, or a pharmaceutically acceptable salt, prodrug, ester, or amide thereof.

3. (Original) A pharmaceutical composition comprising an angiotensin converting enzyme (ACE) inhibitor and an adenosine A_1 receptor antagonist (AA_1RA).

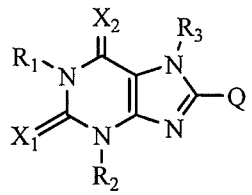
4. (Original) A pharmaceutical composition comprising an angiotensin II receptor blocker (ARB) and an adenosine A_1 receptor antagonist (AA_1RA).

5. (Original) A pharmaceutical composition comprising an angiotensin converting enzyme (ACE) inhibitor, an angiotensin II receptor blocker (ARB), and an adenosine A_1 receptor antagonist (AA_1RA).

6. (Original) The composition of Claim 3, wherein said ACE inhibitor is selected from the group consisting of lisinopril, enalapril, quinapril, ramipril, benazepril, captopril, fosinopril, moexipril, trandolapril, and perindopril, or a pharmaceutically acceptable salt, prodrug, ester, or amide thereof.

7. (Original) The composition of Claims 4, wherein said ARB is selected from the group consisting of losartan, irbesartan, candesartan, telmisartan, eposartan, and valsartan.

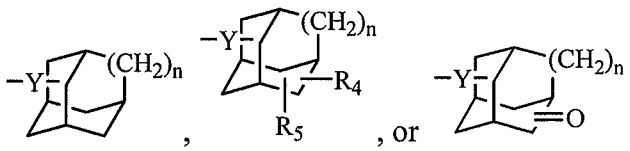
8. (Previously presented) The composition of any one of Claims 1, 3, or 4, wherein said AA_1RA is a xanthine-derivative compound of Formula I or a pharmaceutically acceptable salt thereof,

(I) 

wherein

each of X_1 and X_2 independently represents oxygen or sulfur;

Q represents:

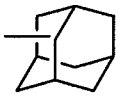


where Y represents a single bond or alkylene having 1 to 4 carbon atoms, n represents 0 or 1;

each of R_1 and R_2 independently represents hydrogen, lower alkyl, allyl, propargyl, or hydroxy-substituted, oxo-substituted or unsubstituted lower alkyl, and R_3 represents hydrogen or lower alkyl, or

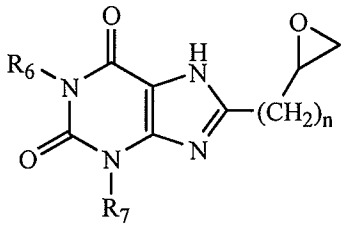
R_4 and R_5 are the same or different and each represent hydrogen or hydroxy, and when both R_4 and R_5 are hydrogen, at least one of R_1 and R_2 is hydroxy-substituted or oxo-substituted lower alkyl,

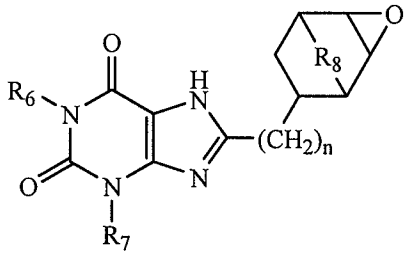
provided that when Q is



then R_1, R_2 and R_3 are not simultaneously methyl,

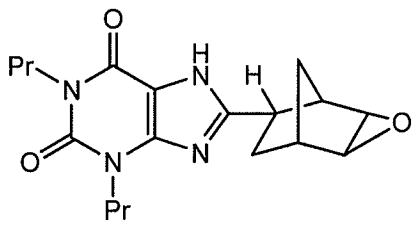
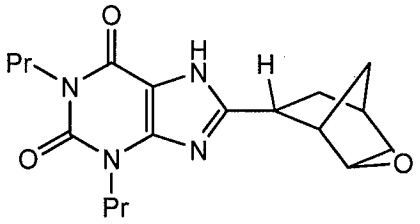
or wherein said AA_1RA is a xanthine epoxide-derivative compound of Formula II or Formula III, or a pharmaceutically acceptable salt thereof,

(II) 

(III) 

wherein R_6 and R_7 are the same or different, and can be hydrogen or an alkyl group of 1-4 carbons, R_8 is either oxygen or $(CH_2)_{1-4}$, and n=0-4.

9. (Original) The composition of Claim 8, wherein said AA_1RA is selected from the group consisting of 8-(noradamantan-3-yl)-1,3-dipropylxanthine; 1,3-Diallyl-8-(3-noradamantyl)xanthine, 3-allyl-8-(3-noradamantyl)-1-propargylxanthine, 8-(trans-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl) -1,3-dipropylxanthine, 8-(cis-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl)-1,3-dipropylxanthine, 8-(trans-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl)-1-(2-oxopropyl)-3-

propylxanthine, 1-(2-hydroxypropyl)-8-(trans-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl)-3-propylxanthine,  , and  or a pharmaceutically acceptable salt thereof.

10. (Original) A method of treating cardiovascular disease comprising identifying a patient in need of such treatment, and administering a pharmaceutical composition of Claim 1 to said patient.

11. (Original) The method of Claim 10, wherein said cardiovascular disease is congestive heart failure, hypertension, asymptomatic left ventricular dysfunction, or coronary artery disease.

12. (Original) The method of Claim 10, wherein said patient is in need of after-load reduction.

13. (Original) The method of Claim 10, wherein said patient requires additional diuretic therapy or is refractory to diuretic therapy.

14. (Original) A method of treating cardiovascular disease or renal disease comprising identifying a patient in need of such treatment, and administering a pharmaceutical composition of any one of Claims 3-5 to said patient.

15. (Original) The method of Claim 14, wherein said patient suffers from cardiovascular disease selected from congestive heart failure, hypertension, asymptomatic left ventricular dysfunction, or acute myocardial infarction, or wherein said patient is in need of after-load reduction, or wherein said patient is refractory to diuretic therapy.

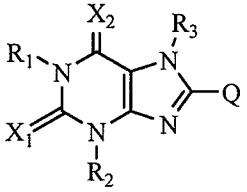
16. (Original) The method of Claim 14, wherein said renal disease is renal hypertrophy, renal hyperplasia, microproteinuria, proteinuria, diabetic nephropathy, contrast-mediated nephropathy, toxin-induced renal injury, or oxygen free-radical mediated nephropathy.

17. (Original) A method of treating alkalosis comprising identifying a patient in need thereof and administering an adenosine A_1 receptor antagonist (AA_1RA) to said patient.

18. (Original) The method of Claim 17, wherein said alkalosis is metabolic alkalosis or respiratory alkalosis.

19. (Original) The method of Claim 17, wherein said patient has edema, is on diuretic therapy, or suffers from acid loss through the patient's upper gastrointestinal tract.

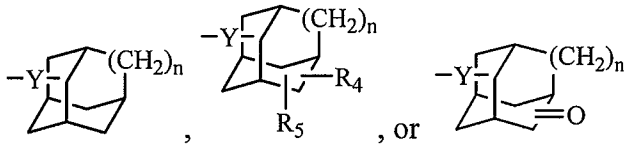
20. (Previously presented) The method of Claim 17, wherein said AA_1RA is a xanthine-derivative compound of Formula I or a pharmaceutically acceptable salt thereof,

(I) 

wherein

each of X_1 and X_2 independently represents oxygen or sulfur;

Q represents:

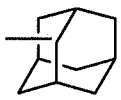


where Y represents a single bond or alkylene having 1 to 4 carbon atoms, n represents 0 or 1;

each of R_1 and R_2 independently represents hydrogen, lower alkyl, allyl, propargyl, or hydroxy-substituted, oxo-substituted or unsubstituted lower alkyl, and R_3 represents hydrogen or lower alkyl, or

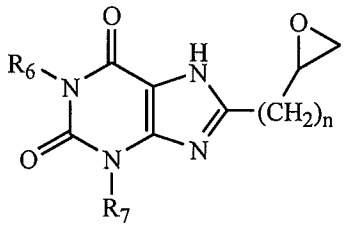
R_4 and R_5 are the same or different and each represent hydrogen or hydroxy, and when both R_4 and R_5 are hydrogen, at least one of R_1 and R_2 is hydroxy-substituted or oxo-substituted lower alkyl,

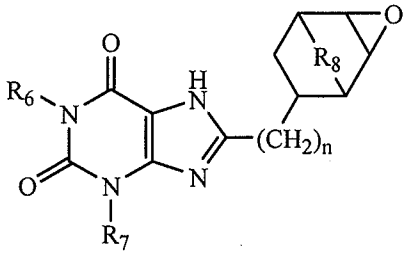
provided that when Q is



then R_1, R_2 and R_3 are not simultaneously methyl,

or wherein said AA_1RA is a xanthine epoxide-derivative compound of Formula II or Formula III, or a pharmaceutically acceptable salt thereof,

(II) 

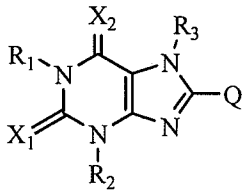
(III) 

wherein R_6 and R_7 are the same or different, and can be hydrogen or an alkyl group of 1-4 carbons, R_8 is either oxygen or $(CH_2)_{1-4}$, and n=0-4.

21. (Original) A method of treating diabetic nephropathy comprising identifying a patient in need thereof and administering an adenosine A_1 receptor antagonist (AA_1RA) to said patient.

22. (Original) The method of Claim 21, wherein said patient is pre-diabetic or is in early stage diabetes.

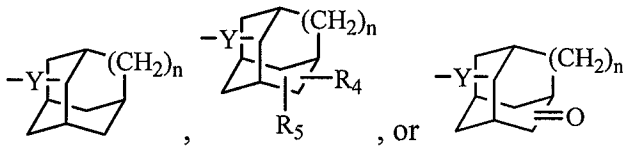
23. (Previously presented) The method of Claim 21, wherein said AA_1RA is a xanthine-derivative compound of Formula I or a pharmaceutically acceptable salt thereof,

(I) 

wherein

each of X_1 and X_2 independently represents oxygen or sulfur;

Q represents:

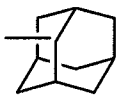


where Y represents a single bond or alkylene having 1 to 4 carbon atoms, n represents 0 or 1;

each of R_1 and R_2 independently represents hydrogen, lower alkyl, allyl, propargyl, or hydroxy-substituted, oxo-substituted or unsubstituted lower alkyl, and R_3 represents hydrogen or lower alkyl, or

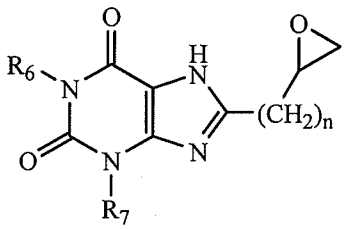
R_4 and R_5 are the same or different and each represent hydrogen or hydroxy, and when both R_4 and R_5 are hydrogen, at least one of R_1 and R_2 is hydroxy-substituted or oxo-substituted lower alkyl,

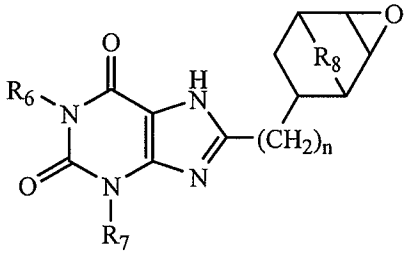
provided that when Q is



then R_1, R_2 and R_3 are not simultaneously methyl,

or wherein said AA_1RA is a xanthine epoxide-derivative compound of Formula II or Formula III, or a pharmaceutically acceptable salt thereof,

(II) 

(III) 

wherein R_6 and R_7 are the same or different, and can be hydrogen or an alkyl group of 1-4 carbons, R_8 is either oxygen or $(CH_2)_{1-4}$, and n=0-4.

24. (Original) The method of Claim 21, further comprising administering a compound selected from the group consisting of a protein kinase C inhibitor, an inhibitor of tissue proliferation, an antioxidant, an inhibitor of glycosylation, and an endothelin B receptor inhibitor.

25. (Original) The method of Claim 21, wherein said treating comprises preventing, reversing, or ameliorating a disease selected from the group consisting of renal hypertrophy, renal hyperplasia, microproteinuria, and proteinuria.

26. (Previously presented)A method of treating cardiovascular disease in a patient, comprising:

identifying a patient in need of treatment for cardiovascular disease; and

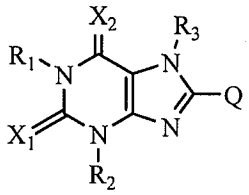
administering an adenosine A1 receptor antagonist in conjunction with a beta blocker to said patient.

27. (Previously presented) The method of Claim 26, wherein said cardiovascular disease is congestive heart failure, hypertension, asymptomatic left ventricular dysfunction, or coronary artery disease.

28. (Previously presented) The method of Claim 26, wherein said patient is in need of after-load reduction.

29. (Previously presented) The method of Claim 26, wherein said patient requires additional diuretic therapy or is refractory to diuretic therapy.

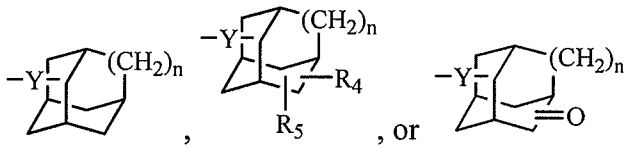
30. (Previously presented) The method of Claim 26, wherein said AA_1RA is a xanthine-derivative compound of Formula I or a pharmaceutically acceptable salt thereof,

(I) 

wherein

each of X_1 and X_2 independently represents oxygen or sulfur;

Q represents:



where Y represents a single bond or alkylene having 1 to 4 carbon atoms, n represents 0 or 1;

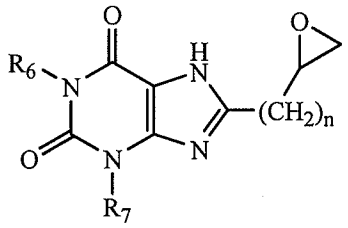
each of R_1 and R_2 independently represents hydrogen, lower alkyl, allyl, propargyl, or hydroxy-substituted, oxo-substituted or unsubstituted lower alkyl, and R_3 represents hydrogen or lower alkyl, or

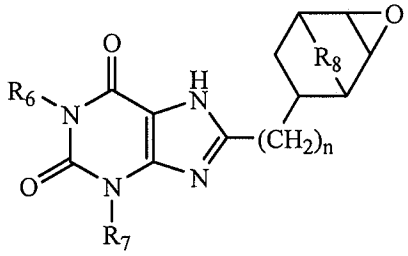
R_4 and R_5 are the same or different and each represent hydrogen or hydroxy, and when both R_4 and R_5 are hydrogen, at least one of R_1 and R_2 is hydroxy-substituted or oxo-substituted lower alkyl,

provided that when Q is

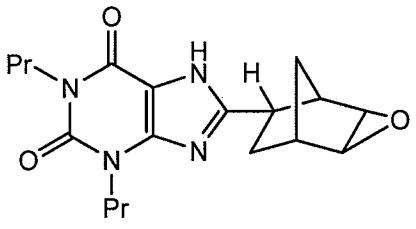
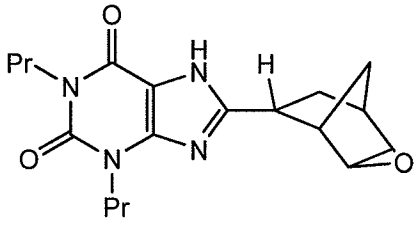
then R_1, R_2 and R_3 are not simultaneously methyl,

or wherein said AA_1RA is a xanthine epoxide-derivative compound of Formula II or Formula III, or a pharmaceutically acceptable salt thereof,

(II) 

(III) 

wherein R_6 and R_7 are the same or different, and can be hydrogen or an alkyl group of 1-4 carbons, R_8 is either oxygen or $(CH_2)_{1-4}$, and n=0-4.

31. (Previously presented) The method of Claim 30, wherein said AA_1RA is selected from the group consisting of 8-(noradamantan-3-yl)-1,3-dipropylxanthine; 1,3-Diallyl-8-(3-noradamantyl)xanthine, 3-allyl-8-(3-noradamantyl)-1-propargylxanthine, 8-(trans-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl) -1,3-dipropylxanthine, 8-(cis-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl)-1,3-dipropylxanthine, 8-(trans-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl)-1-(2-oxopropyl)-3-propylxanthine, 1-(2-hydroxypropyl)-8-(trans-9-hydroxy-3-tricyclo[3.3.1.$0^{3,7}$]nonyl)-3-propylxanthine,  , and 
or a pharmaceutically acceptable salt thereof.

32. (Previously presented) The method of Claim 26, wherein said AA_1RA is KW-3902, or a pharmaceutically acceptable salt, ester, amide, or metabolite thereof.

33. (Previously presented) The method of Claim 26, wherein said beta blocker is selected from the group consisting of acebutolol hydrochloride, atenolol, betaxolol hydrochloride, bisoprolol fumarate, carteolol hydrochloride, esmolol hydrochloride, metoprolol, metoprolol tartrate, nadolol, penbutolol sulfate, pindolol, propranolol hydrochloride, succinate, and timolol maleate, or a pharmaceutically acceptable salt, prodrug, ester, or amide thereof.

34. (Previously presented) The method of Claim 26, wherein said AA_1RA and said beta blocker are administered substantially simultaneously.